

IN THE CLAIMS

I. Amendments to Pending Claims

Please substitute pending claims 1, 60-61, 64, 104, 115-116, and 119 with the corresponding amended claims, as shown below.

1. (Amended) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises:

- a) — about 0.1% to about 10% testosterone;
- b) — about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;
- c) — about 0.1 % to about 5 % isopropyl myristate;
- d) — about 1 % to about 5 % sodium hydroxide; and
- e) — about 0.1 % to about 5 % gelling agent; and

wherein the percentages are weight to weight of the composition, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a circulating serum concentration of the testosterone greater than about 400 ng testosterone per dL serum during a time period beginning about 2 hours after administration and ending about 24 hours after administration such that the method results in at least one of the following:

(a) a serum testosterone C_{avg} of about 223 to about 797 ng/dL on the first day of administration to the subject;

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(b) a serum testosterone C_{max} of about 288 to about 1178 ng/dL on the first day of administration to the subject;

(c) a serum testosterone C_{min} of about 92 to about 419 ng/dL on the first day of administration to the subject;

(d) a serum testosterone C_{avg} of about 304 to about 1086 ng/dL by the thirtieth consecutive day of administration to the subject;

(e) a serum testosterone C_{max} of about 410 to about 1682 ng/dL by the thirtieth consecutive day of administration to the subject;

(f) a serum testosterone C_{min} of about 212 to about 738 ng/dL by the thirtieth consecutive day of administration to the subject; or

(g) a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.

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60. (Amended) The method of claim 1, wherein the composition penetration enhancer comprises about 0.25 % to about 2.5 % isopropyl myristate.

61. (Amended) The method of claim 1, wherein the composition penetration enhancer comprises about 0.5 % isopropyl myristate.

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64. (Amended) The method of claim 1, wherein the composition further comprises about 40 % to about 90 % alcohol.

104. (Amended) A method of transdermally delivering testosterone to a male subject in need thereof, comprising:

(a) preparing a hydroalcoholic gel composition which comprises

1) ~~about 0.1 % to about 10 % testosterone;~~

2) ~~about 30 % to about 98 % alcohol selected from the group consisting of ethanol, and isopropanol;~~

3) ~~about 0.1 % to about 5 % isopropyl myristate;~~

4) ~~about 1 % to about 5 % sodium hydroxide; and~~

5) ~~about 0.1 % to about 5 % gelling agent; , at least one penetration enhancer, at least one alcohol, and at least one gelling agent, and~~

(b) applying the composition to a selected area of skin of the subject in an amount effective to treat hypogonadism in the subject;

~~wherein the percentages are weight to weight of the composition, and wherein the composition does not comprise a glycol or a glycerol.~~

115. (Amended) The method of claim 104, wherein the composition penetration enhancer comprises about 0.25% to about 2.5 % isopropyl myristate.

116. (Amended) The method of claim 104, wherein the composition penetration enhancer comprises about 0.5% isopropyl myristate.

119. (Amended) The ~~method~~ of claim 104, wherein the composition further comprises about 40% to about 90% alcohol.

II. *New Claims*

Please add claims 152 to 165 as follows.

152. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, and at least one alcohol; wherein upon once daily administration of the composition to a selected area of skin of a subject, the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the administration results in at least one of the following:

- (a) a serum testosterone C_{avg} of about 304 to about 1086 ng/dL by the thirtieth consecutive day of administration to the subject;
- (b) a serum testosterone C_{max} of about 410 to about 1682 ng/dL by the thirtieth consecutive day of administration to the subject;
- (c) a serum testosterone C_{min} of about 212 to about 738 ng/dL on the thirtieth consecutive day of administration to the subject; or
- (d) a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.

153. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent; wherein upon once daily administration of the composition to a selected area of skin of a subject, the composition is capable of providing a serum testosterone net $AUC_{(0-24)}$ of

about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.

154. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent;

wherein the penetration enhancer comprises a functional derivative of a fatty acid, and

wherein the composition does not comprise a glycol or a glycerol.

155. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent;

wherein the penetration enhancer is selected from the group consisting of isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, terpene, and combinations of any of the foregoing.

156. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent;

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wherein the penetration enhancer is selected such that when the composition is applied to skin of a subject, the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a circulating serum concentration of the testosterone greater than about 400 ng testosterone per dl serum during a time period beginning about 2 hours after administration and ending about 24 hours after administration; and

wherein the composition does not comprise a glycol or a glycerol.

157. (New) A pharmaceutical composition comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent;

wherein the penetration enhancer is selected such that when the composition is applied to skin of a subject, the testosterone is absorbed into the bloodstream of the subject at a rate and duration that maintains a circulating serum concentration of the testosterone greater than about 400 ng testosterone per dl serum during a time period beginning about 2 hours after administration and ending about 24 hours after administration; and

wherein the method results in a steady-state testosterone 24-hour pharmacokinetics profile in the subject, wherein the profile exhibits a first testosterone serum concentration upon administration of the composition and exhibits a second testosterone serum concentration having a small increase at about two hours after application compared to the first testosterone serum concentration, followed by a decrease to a third testosterone serum concentration that remains relatively constant for the remainder of the day; and

wherein the composition does not comprise a glycol or a glycerol.

158. (New) A pharmaceutical composition in the form of a hydroalcoholic gel, comprising: testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent;

wherein the penetration enhancer is selected from the group consisting of isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, terpene, and combinations of any of the foregoing; and

wherein upon once daily administration of the composition to a selected area of skin of a subject, the composition is capable of providing a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.

159. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone C_{avg} of about 223 to about 797 ng/dL on the first day of administration to the subject.

160. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone C_{\max} of about 288 to about 1178 ng/dL on the first day of administration to the subject.

161. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone C_{\min} of about 92 to about 419 ng/dL on the first day of administration to the subject.

162. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results

in a serum testosterone C_{avg} of about 304 to about 1086 ng/dL by the thirtieth consecutive day of administration to the subject.

163. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone C_{max} of about 410 to about 1682 ng/dL by the thirtieth consecutive day of administration to the subject.

164. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone C_{min} of about 212 to about 738 ng/dL by the thirtieth consecutive day of administration to the subject.

165. (New) A method of transdermally delivering testosterone to a male subject in need thereof, comprising: Administering to the subject a pharmacologically effective amount of a composition to a selected area of skin of the subject, wherein the composition is a hydroalcoholic gel and free of a glycol or a glycerol, and comprises testosterone, at least one

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penetration enhancer, at least one alcohol, and at least one gelling agent, wherein the testosterone is absorbed into the bloodstream of the subject at a rate and duration such that the method results in a serum testosterone net $AUC_{(0-24)}$ of about 240 to about 476 (nmol*h/L) by the thirtieth consecutive day of administration to the subject.

CONCLUSION

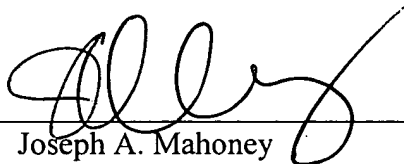
With entry of the above Supplemental Amendment, it is respectfully submitted that the pending claims are in condition for allowance. Applicants request an interview with the Examiner to discuss the pending claims.

None of Applicants' amendments or cancellations are to be construed as dedicating any such subject matter to the public, and Applicants reserve all rights to pursue any such subject matter in this or a related patent application. The amendments are made solely to expedite prosecution.

The Examiner is invited to call Applicant's undersigned attorney at (312) 701-8979 for questions and to expedite prosecution.

Respectfully submitted,

By: _____


Joseph A. Mahoney
Reg. No. 38,956

MAYER, BROWN, ROWE & MAW
P.O. BOX 2828
CHICAGO, ILLINOIS 60690-2828
(312) 701-8979
Dated: June 3, 2003